

REMARKS

The Abstract in the original application has been replaced with a new Abstract. The new Abstract contains less than 150 words.

Claims 1-40 are active in the present application. Claims 3-4 and 29-34 have been amended to remove multiple dependencies. Support for new Claims 35-40 is found in the original Claims 1-34. Claims 16 and 24 have been corrected for clarity. No new matter is added. An action on the merits and allowance of claims is solicited.

Respectfully submitted,

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Marked-Up Copy Serial No: <u>09/830,559</u> Amendment Filed on: <u>July 16, 2001</u>

IN THE CLAIMS

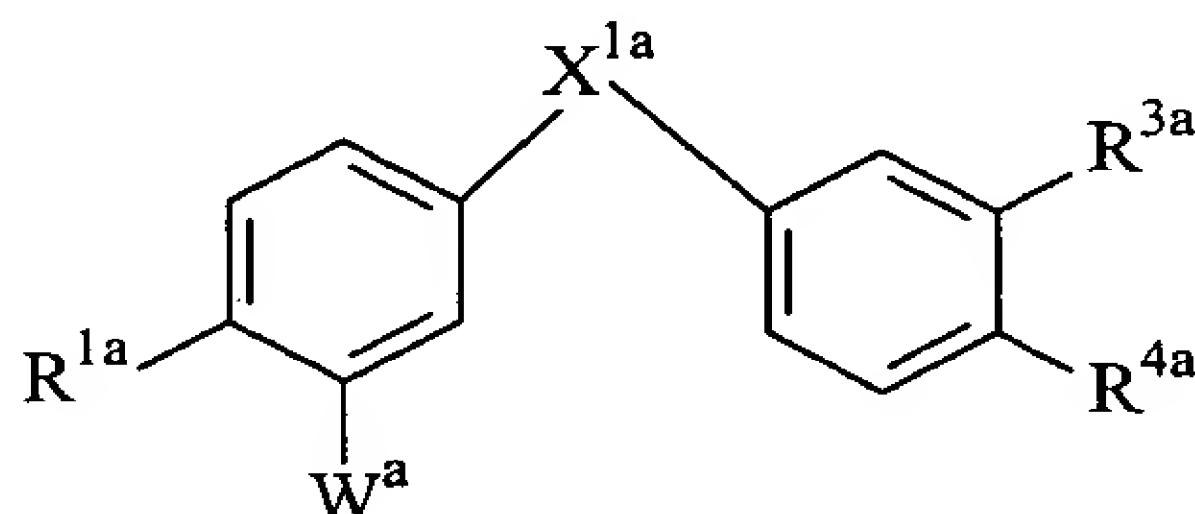
--3. (Amended) A compound or a salt thereof according to Claim 1 [or 2], wherein N₁ constituting the pharmacophore is a nitrogen atom of unsubstituted or substituted amino, ammonium, amido, thioamido, ureido, isoureido, amidino, guanidino, thioureido, hydrazino or hydrazono group to which one or more hydrogen atoms are bonded, a carbon atom of ethenyl group to which a hydrogen atom is bonded, an oxygen atom of carbonyl group, a sulfur atom of thiocarbonyl group, a nitrogen atom of unsubstituted or substituted imino group, an oxygen atom of sulfonyl group, an oxygen atom of sulfonyloxy group, an oxygen atom of sulfo group, an oxygen atom of sulfinyl group, an oxygen atom of carboxyl group, an oxygen atom of ether, a sulfur atom of thioether, a sulfur atom of mercapto group, an oxygen atom of hydroxyl group, an oxygen atom of ester or a nitrogen atom of unsubstituted or substituted nitrogen-containing heterocyclic group; N₃ is an oxygen atom of carbonyl group, a sulfur atom of thiocarbonyl group, a nitrogen atom of unsubstituted or substituted imino group, an oxygen atom of sulfo group, an oxygen atom of sulfonyl group, an oxygen atom of sulfo group, an oxygen atom of sulfonyloxy group, an oxygen atom of carboxyl group, an oxygen atom of ether, a sulfur atom of thioether, an oxygen atom of hydroxyl group, an oxygen atom of ester, a nitrogen atom of unsubstituted or substituted nitrogen-containing heterocyclic group to which no hydrogen atom is combined, a nitrogen atom of sulfonamido

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group or a nitrogen atom of acylsulfonamido group; and each of N₂, N₄ and N₅ is an arbitrary carbon atom constituting a carbon atom of alkyl group, a carbon atom of alkenyl group, a carbon atom of aryl group and a carbon atom of alkoxy group.

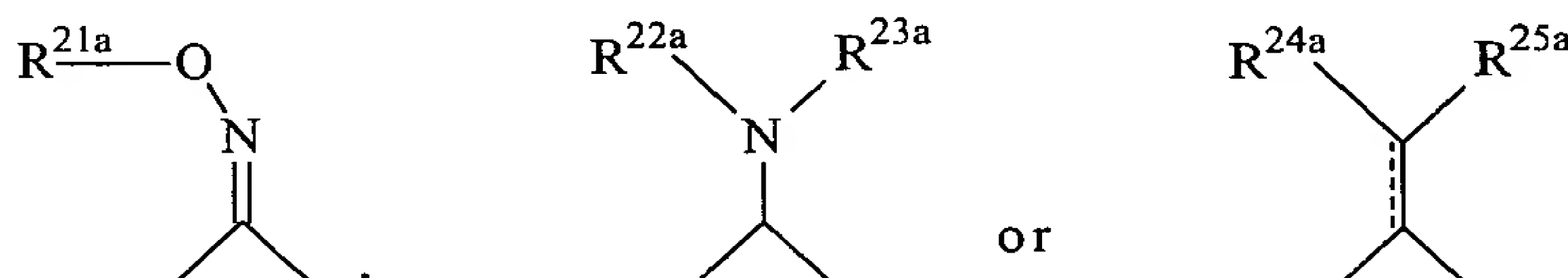
4. (Amended) A compound or a salt thereof according to [any one of Claims 1 to 3] Claim 1, wherein a compound having an atom corresponding to N₃ and atoms corresponding to two or more atoms selected from N₁, N₂, N₄ and N₅ among the atoms N₁, N₂, N₃, N₄ and N₅ constituting a pharmacophore, and, in the optimized three-dimensional structure thereof, the interatomic distances between the atom corresponding to N₃ and the two or more atoms selected from N₁, N₂, N₄ and N₅ are the atomic distances of a pharmacophore has an activity of antagonistically inhibiting the binding between AP-1 (activator protein-1) and a recognition sequence thereof.

16. (Amended) A benzene derivative represented by the following formula:



wherein R^{1a} represents a halogen atom, a cyano group, a nitro group, an unprotected or protected hydroxyl group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; R^{3a} and R^{4a} may be the same or different represent a halogen atom, a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a

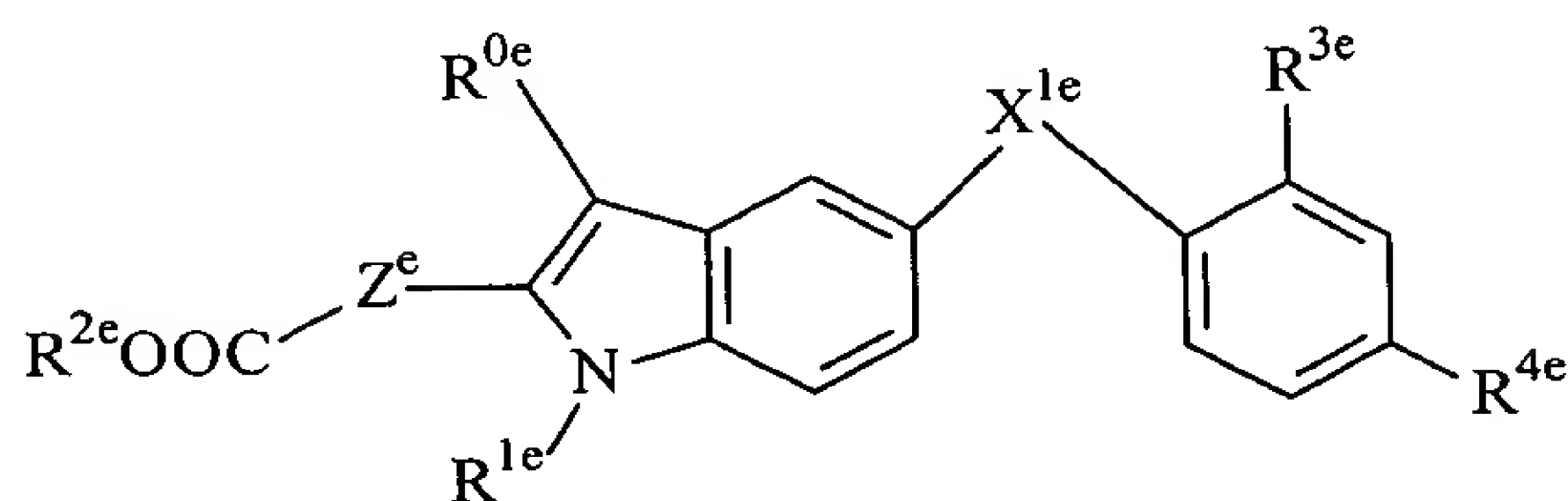
mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; X^{1a} represents $-C(O)-$, $-CH(OH)-$, $-CH_2-$ or a group of the following formula:



wherein R^{21a} represents an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, acyl or heterocycle-lower alkyl group; R^{22a} and R^{23a} may be the same or different represent a hydrogen atom or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, acyl, carbamoyl, alkylsulfinyl, alkylsulfonyl, arylsulfonyl or heterocyclic group; R^{24a} and R^{25a} may be the same or different represent a hydrogen atom, a halogen atom, a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; and the double line of which one line is a broken line represents a single bond or a double bond and W^a represents $-Z^a-COR^{26a}$, $-Z^a-COOR^{2a}$, $-O-CH_2COOR^{2a}$ or $-O-CH_2CH_2COOR^{2a}$ (wherein Z^a represents $-(CH_2)_{n^a}-$ (n^a is [0,] 1, 2 or 3), $-CH_2CH(CH_3)-$, $-CH=CH-$ or $-CH_2CH=CH-$; R^{2a} represents a hydrogen atom or a protecting group for carboxyl group; and R^{26a} represents $-NHR^{27a}$ or $-NHSO_2R^{28a}$ [in which] (R^{27a} and R^{28a} independently represent an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl or aralkyl group));

or a salt thereof.

24. (Amended) A benzene derivative represented by the following general formula:

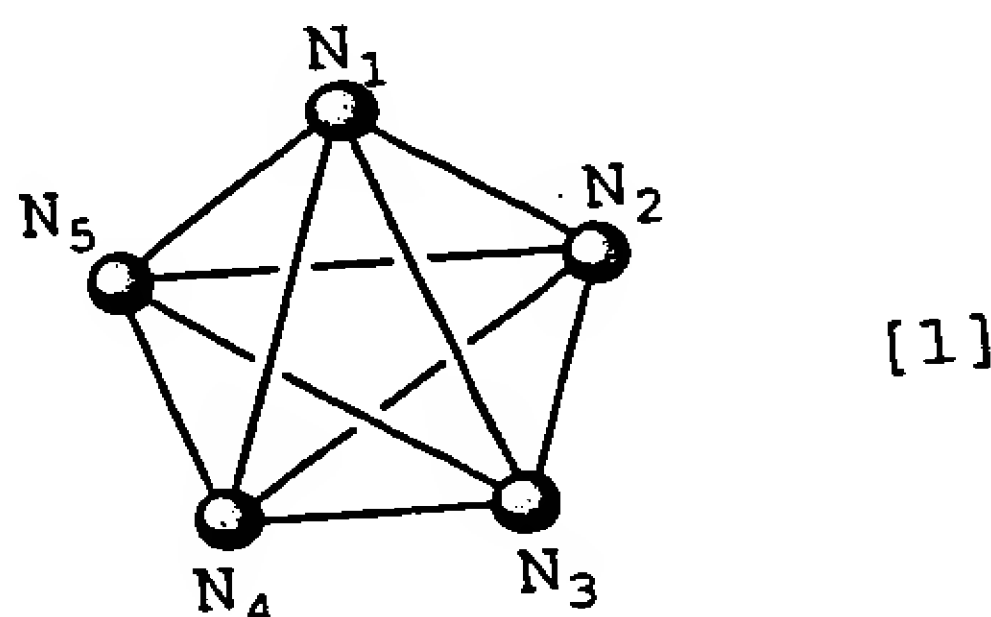


wherein R^{0e} represents a hydrogen atom, a halogen atom, a nitro group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, acyl, alkoxycarbonyl, aryloxycarbonyl, alkylsulfonylamino or arylsulfonylamino group; R^{1e} represents an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, acyl, alkoxycarbonyl, aryloxycarbonyl or alkylsulfonyl group; R^{2e} represents a hydrogen atom or a protecting group for carboxyl group; R^{3e} and R^{4e} may be the same or different represent a hydrogen atom, a halogen atom, an unprotected or protected hydroxyl group, a unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, alkylthio, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group, provided that both R^{3e} and R^{4e} cannot simultaneously be a hydrogen atom; X^{1e} represents $-C(O)-$, $-CH(OH)-$ or $-CH_2-$; and Z^e represents $-(CH_2)_n-$ (n^e represents 0, 1 or 2) or $-CH=CH-$;

or a salt thereof.

29. (Amended) A compound or a salt thereof according to [any one of Claims 5 to 28] Claim 9, wherein said compound [according to any one of Claims 5 to 28] is a compound that has an activity of antagonistically inhibiting the combination between AP-1 and a recognition sequence thereof.

30. (Amended) [A compound or a salt thereof according to Claim 1] A compound comprising the atom corresponding to N₃ and the two or more atoms selected from N₁, N₂, N₄ and N₅, said atoms constitute the pharmacophore represented by the following formula 1:



wherein N₁ represents an atom to which a donative hydrogen atom in a hydrogen-bond donating group is bonded or a hydrogen-bond accepting atom in a hydrogen-bond accepting group; N₃ represents a hydrogen-bond accepting atom in a hydrogen-bond accepting group; and N₂, N₄ and N₅ independently represent an arbitrary carbon atom constituting a hydrophobic group and the distance between N₁ and N₂ is not less than 5 angstroms and not more than 12 angstroms, the distance between N₁ and N₃ is not less than 9 angstroms and not more than 15 angstroms, the distance between N₁ and N₄ is not less than 3 angstroms and not more than 13 angstroms, the distance between N₁ and N₅ is not less than 8 angstroms and not more than 16 angstroms, the distance between N₂ and N₃ is not less than 3 angstroms and not more than 10 angstroms, the distance between N₂ and N₄ is not less than 6 angstroms and not more than 14 angstroms, the distance between N₂ and N₅ is not less than 9 angstroms and not more than 14 angstroms, the distance between N₃ and N₄ is not less than 4 angstroms and not more than 11 angstroms, the distance between N₃ and N₅ is not less than 3 angstroms and not more than 10 angstroms, the distance between N₄ and N₅ is not less than 4 angstroms and not

more than 9 angstroms; and, in the optimized three-dimensional structure thereof, the distances between the atom corresponding to N₃ and the two or more atoms selected from N₁, N₂, N₄ and N₅ are the interatomic distances in the pharmacophore; and a salt thereof, wherein the compound conforming to a pharmacophore [of Claim 1] is a peptide or a benzene derivative according to [any one of Claims 5 to 28] Claim 9.

31. (Amended) A method for inhibiting AP-1 which comprises administering a compound or a salt thereof according to [any one of Claims 1 to 30] Claim 1.

32. (Amended) An agent for preventing and treating a disease into which an excessive expression of AP-1 participates, which comprises a compound or a salt thereof according to [any one of Claims 1 to 30] Claim 1.

33. (Amended) An agent for preventing and treating an autoimmune disease, which comprises a compound or a salt thereof according to [any one of Claims 1 to 30] Claim 1.

34. (Amended) An AP-1 inhibitor comprising a compound or a salt thereof according to [any one of Claims 1 to 30] Claim 1.

Claims 35-40 (New).--

IN THE ABSTRACT

--New.--